PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
TERESA A. LAVOIE
FISH & RICHARDSON P.C.
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing *(day/month/year)*	15 FEB 2011
Applicant's or agent's file reference 253240012WO1	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 10/53484	International filing date *(day/month/year)* 21 October 2010 (21.10.2010)
Applicant CUREMARK LLC	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 338 82 70

For more detailed instructions, see *PCT Applicant's Guide*, International Phase, paragraphs 9.001 – 9.011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. Following the expiration of 30 months from the priority date, these comments will also be made available to the public.

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer Lee W. Young PCT Helpdesk: 571-272-4300 Telephone No. PCT OSP: 571-272-7774

Form PCT/ISA/220 (July 2010)

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 253240012WO1	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US 10/53484	International filing date *(day/month/year)* 21 October 2010 (21.10.2010)	(Earliest) Priority Date *(day/month/year)* 21 October 2009 (21.10.2009)
Applicant CUREMARK LLC		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

   b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

   c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

3. ☒ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

   ☒ the text is approved as submitted by the applicant.

   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   ☒ the text is approved as submitted by the applicant.

   ☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

   a. the figure of the **drawings** to be published with the abstract is Figure No. _____

   ☐ as suggested by the applicant.

   ☐ as selected by this Authority, because the applicant failed to suggest a figure.

   ☐ as selected by this Authority, because this figure better characterizes the invention.

   b. ☐ none of the figures is to be published with the abstract.

International application No.
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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-16, and 34-38 directed to a method for treatment or prevention of influenza in a mammal or bird, comprising administering a therapeutically effective amount of a pharmaceutical composition comprising one or more digestive enzymes.

Group II: claims 17-28, directed to a method of diagnosing a patient as immune-compromised, comprising: a) obtaining a fecal sample from the patient; b) determining a level of chymotrypsin present in the fecal sample; and c) diagnosing the patient as having a compromised immune system if the determined fecal chymotrypsin level is less than a control level.

- Please see extra sheet for continuation -

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-16 and 34-38

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US2010/053484 15.02.2011

International application No.
PCT/US 10/53484

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 38/46 (2011.01)
USPC - 514/3.7
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC -- 514/3.7, 514/2, 514/3; IPC(8) -- A61K 38/46

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST -- PGPB,USPT,USOC,EPAB,JPAB; Dialog Classic Files -- 654, 652, 349, 35, 65, 155; USPTO Web Page; PCT Patentscope; Google Scholar; Search terms -- treatment, prevention, influenza A, H1N1, trypsin, chymotrypsin, porcine pancreatic enzymes, amylase, lipase, antiviral therapy, capsule, dosages

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	WO 90/002562 A1 (SUTTON et al.) 22 March 1990 (22.03.1990) pg 2, para 2-3; pg 3, para 2-3; pg 4, para 5 -- pg 5, para 4; pg 10, para 1; pg 13, para 3	1-5, 7-9, 12, 16 --- 6, 10, 11, 13-15, 38
X	US 2002/0141987 A1 (BJARNASON) 03 October 2002 (03.10.2002) para [0001], [0007], [0013], [0020], [0026], [0031], [0048], [0049], [0054]	34-37
Y	US 2005/0281772 A1 (BROMLEY et al.) 22 December 2005 (22.12.2005) para [0281], [0455]	6, 10
Y	US 5,106,616 A (McANALLEY et al.) 21 April 1992 (21.04.1992) col 12, ln 5-7; col 17, ln 6-17	11, 15
Y	US 2003/0104045 A1 (VIRTANEN et al.) 05 June 2003 (05.06.2003) para [0070]	11, 15
Y	US 2009/0232789 A1 (FALLON) 17 September 2009 (17.09.2009) para [0019], [0035]-[0042], [0049], [0050], Fig 4	13-15, 38

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 January 2011 (28.01.2011)	15 FEB 2011
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

International application No.
PCT/US 10/53484

Continuation of Box III: Lack of Unity of Invention

Group III: claims 29, 30 and 33, directed to a composition comprising one or more digestive enzymes comprising at least one lipase and at least one protease, wherein the ratio of proteases to lipases ranges from about 1:1 to about 20:1.
Group IV: claims 31-33, directed to a pharmaceutical composition comprising at least one amylase, a mixture of proteases comprising trypsin and chymotrypsin and at least one lipase.
Group V: claim 39, directed to a method for sanitizing or disinfecting a surface to reduce the amount of influenza virus thereon, comprising applying to the surface a composition comprising one or more digestive enzymes.
Group VI: claim 40, directed to a method for reducing the amount of influenza virus present on a skin region, tissue, or wound of a mammal or bird comprising applying to the skin region, tissue, or wound a composition comprising one or more digestive enzymes.

The inventions listed as Groups I - VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of the Group I claims is a method for treatment or prevention of influenza in a mammal or bird, comprising administering a therapeutically effective amount of a pharmaceutical composition comprising one or more digestive enzymes. The special technical feature of the Group II claims is a method of diagnosing a patient as immune-compromised, comprising: a) obtaining a fecal sample from the patient; b) determining a level of chymotrypsin present in the fecal sample; and c) diagnosing the patient as having a compromised immune system if the determined fecal chymotrypsin level is less than a control level. The special technical feature of the Group III claims is a composition comprising one or more digestive enzymes comprising at least one lipase and at least one protease, wherein the ratio of proteases to lipases ranges from about 1:1 to about 20:1. The special technical feature of the Group IV claims is a pharmaceutical composition comprising at least one amylase, a mixture of proteases comprising trypsin and chymotrypsin and at least one lipase. The special technical feature of the Group V claims is a method for sanitizing or disinfecting a surface to reduce the amount of influenza virus thereon, comprising applying to the surface a composition comprising one or more digestive enzymes. The special technical feature of the Group VI claims is a method for reducing the amount of influenza virus present on a skin region, tissue, or wound of a mammal or bird comprising applying to the skin region, tissue, or wound a composition comprising one or more digestive enzymes.

There is no common technical element shared by all of the above groups. Groups I, III and IV share the common technical element of a pharmaceutical composition comprising digestive enzymes, and Groups III and IV share the further common technical element of said enzymes comprising at least one protease and at least one lipase. Groups I, II, V and VI share the common technical element of being related to influenza virus. Groups I and II also being related to evaluating fecal chymotrypsin levels. Groups V and VI share the common technical element of being related to the reduction of the amount of influenza virus being present on a surface. The forgoing common technical elements do not represent an improvement over the prior art of US 2009/0186012 A1 to Hawkins, which discloses administration to a protease to a subject for the treatment of influenza (see para [0023], [0024], [0046]). Additionally, US 2009/0117180 A1 to Ortenzi et al. discloses pharmaceutical compositions comprising proteases, including trypsin and chymotrypsin, as well as lipases and amylases (see para [0029], para [0032] and [0020]) Further, US 2008/0108099 A1 to Donndelinger discloses methods for diagnosing chronic diarrhea (abstract), including viral (para [0021]), wherein the characterization includes the assessment of enzymes in samples, including chymotrypsin (para [0023]), wherein the samples may be stool samples (para [0024]). Finally, US 2008/0193389 A1 to Bott et al. discloses the application of a protease (glycodendrimer protease; abstract) to a surface, including skin (para [0013]) to reduce binding of a microorganism such as influenza (para [0063]). Therefore, the inventions of Groups I-VI lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: TERESA A. LAVOIE
FISH & RICHARDSON P.C.
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	15 FEB 2011
Applicant's or agent's file reference 253240012WO1	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 10/53484	21 October 2010 (21.10.2010)	21 October 2009 (21.10.2009)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - A61K 38/46 (2011.01)
USPC - 514/3,7

Applicant CUREMARK LLC

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [X] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	30 January 2011 (30.01.2011)	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/53484

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:

   a. (means)

   ☐ on paper

   ☐ in electronic form

   b. (time)

   ☐ in the international application as filed

   ☐ together with the international application in electronic form

   ☐ subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/53484

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the appicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-16, and 34-38 directed to a method for treatment or prevention of influenza in a mammal or bird, comprising administering a therapeutically effective amount of a pharmaceutical composition comprising one or more digestive enzymes.
Group II: claims 17-28, directed to a method of diagnosing a patient as immune-compromised, comprising: a) obtaining a fecal sample from the patient; b) determining a level of chymotrypsin present in the fecal sample; and c) diagnosing the patient as having a compromised immune system if the determined fecal chymotrypsin level is less than a control level.
Group III: claims 29, 30 and 33, directed to a composition comprising one or more digestive enzymes comprising at least one lipase and at least one protease, wherein the ratio of proteases to lipases ranges from about 1:1 to about 20:1.
Group IV: claims 31-33, directed to a pharmaceutical composition comprising at least one amylase, a mixture of proteases comprising trypsin and chymotrypsin and at least one lipase.
Group V: claim 39, directed to a method for sanitizing or disinfecting a surface to reduce the amount of influenza virus thereon, comprising applying to the surface a composition comprising one or more digestive enzymes.
Group VI: claim 40, directed to a method for reducing the amount of influenza virus present on a skin region, tissue, or wound of a mammal or bird comprising applying to the skin region, tissue, or wound a composition comprising one or more digestive enzymes.

The inventions listed as Groups I - VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of the Group I claims is a method for treatment or prevention of influenza in a mammal or bird, comprising administering a therapeutically effective amount of a pharmaceutical composition comprising one or more digestive enzymes. The special technical feature of the Group II claims is a method of diagnosing a patient as immune-compromised, comprising: a) obtaining a fecal sample from the patient; b) determining a level of chymotrypsin present in the fecal sample; and c) diagnosing the patient as having a compromised immune system if the determined fecal chymotrypsin level is less than a control level. The special technical feature of the Group III claims is a composition comprising one or more digestive enzymes comprising at least one lipase and at least one protease, wherein the ratio of proteases to lipases ranges from about 1:1 to about 20:1. The special technical feature of the Group IV claims is a pharmaceutical composition comprising at least one amylase, a mixture of proteases comprising trypsin and chymotrypsin and at least one lipase. The special technical feature of the Group V claims is a method for sanitizing or disinfecting a surface to reduce the amount of influenza virus thereon, comprising applying to the surface a composition comprising one or more digestive enzymes. The special technical feature of the Group VI claims is a method for reducing the amount of influenza virus present on a skin region, tissue, or wound of a mammal or bird comprising applying to the skin region, tissue, or wound a composition comprising one or more digestive enzymes.

- Please see first continuation sheet -

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-16 and 34-38

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/53484

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	6, 10, 11, 13-15, 38	YES
	Claims	1-5, 7-9, 12, 16, 34-37	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-16, 34-38	NO
Industrial applicability (IA)	Claims	1-16, 34-38	YES
	Claims	NONE	NO

2. Citations and explanations:

Claims 1-5, 7-9, 12 and 16 lack novelty under PCT Article 33(2) as being anticipated by WO 1990/002562 A1 to Sutton et al. (hereinafter "Sutton").

Regarding claim 1, Sutton teaches a method for the treatment or prevention of influenza (pg 3, para 2) in a mammal (pg 3, para 3, human), comprising administering to the mammal (pg 4, para 4-5) a therapeutically effective amount (pg 5, para 3) of a pharmaceutical composition (pg 2, para 3) comprising one or more digestive enzymes (pg 4, para 2-3).

Regarding claim 2, Sutton teaches the method of claim 1 wherein the Influenza (pg 3, para 2) is influenza Type A (pg 10, para 1, Table 3; pg 13, para 3).

Regarding claim 3, Sutton teaches the method of claim 2 where the Influenza Type is Subtype H1N1 (pg 10, para 1, Table 3).

Regarding claim 4, Sutton teaches the method of claim 1 wherein the one or more digestive enzymes (pg 4, para 2-3) comprise proteases (pg 4, para 3, trypsin, chymotrypsin) and papain (pg 4, para 2).

Regarding claim 5, Sutton teaches the method of claim 1 wherein the one or more digestive enzymes (pg 4, para 2-3) comprise one or more pancreatic enzymes (pg 4, para 3, trypsin, chymotrypsin).

Regarding claim 7, Sutton teaches the method of claim 4 wherein the proteases comprise chymotrypsin and trypsin (pg 4, para 3).

Regarding claim 8, Sutton teaches the method of claim 1 wherein the one or more digestive enzymes (pg 4, para 2-3) are, independently, derived from an animal source (pg 4, para 3, trypsin, chymotrypsin) and a plant source (pg 4, para 2, papain).

Regarding claim 9, Sutton teaches the method of claim 1 wherein the mammal is a human (pg 3, para 3).

Regarding claim 12, Sutton teaches the method of claim 1, further comprising treating the mammal (pg 3, para 3, human) with an anti-viral medication (pg 5, para 4).

Regarding claim 16, Sutton teaches the method of claim 1 wherein the pharmaceutical composition (pg 2, para 3) is a dosage formulation (pg 4, para 5 to pg 5, para 2) consisting of capsules (pg 4, para 5 to pg 5, para 1).

Claims 34-37 lack novelty under PCT Article 33(2) as being anticipated by US 2002/0141987 A1 (Bjarnason).

Regarding claim 34, Bjarnason teaches a method for treating a mammal (para [0007], human) exhibiting one or more symptoms (para [0007], [0013], pain) of influenza (para [0026], [0031]) comprising administering to the mammal a therapeutically effective amount (para [0054]) of a composition (para [0020]) comprising one or more digestive enzymes (para [0020], trypsin).

Regarding claim 35, Bjarnason teaches the method of claim 34 where the symptoms of influenza (para [0026], [0031]) consists of body aches (para [0007], [0013], pain).

Regarding claim 36, Bjarnason teaches the method of claim 34 wherein the mammal is a human (para [0007]).

Regarding claim 37, Bjarnason teaches the method of claim 34 wherein the preparation (para [0001], [0020], pharmaceutical composition) is administered orally (para [0048]0 via a dosage formulation consisting of capsules (para [0048]).

SEE CONTINUATION SHEET.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/53484

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
Box IV: Lack of Unity of Invention

There is no common technical element shared by all of the above groups. Groups I, III and IV share the common technical element of a pharmaceutical composition comprising digestive enzymes, and Groups III and IV share the further common technical element of said enzymes comprising at least one protease and at least one lipase. Groups I, II, V and VI share the common technical element of being related to influenza virus. Groups I and II also being related to evaluating fecal chymotrypsin levels. Groups V and VI share the common technical element of being related to the reduction of the amount of influenza virus being present on a surface. The forgoing common technical elements do not represent an improvement over the prior art of US 2009/0186012 A1 to Hawkins, which discloses administration to a protease to a subject for the treatment of influenza (see para [0023], [0024], [0046]). Additionally, US 2009/0117180 A1 to Ortenzi et al. discloses pharmaceutical compositions comprising proteases, including trypsin and chymotrypsin, as well as lipases and amylases (see para [0029], para [0032] and [0020]) Further, US 2008/0108099 A1 to Donndelinger discloses methods for diagnosing chronic diarrhea (abstract), including viral (para [0021]), wherein the characterization includes the assessment of enzymes in samples, including chymotrypsin (para [0023]), wherein the samples may be stool samples (para [0024]). Finally, US 2008/0193389 A1 to Bott et al. discloses the application of a protease (glycodendrimer protease; abstract) to a surface, including skin (para [0013]) to reduce binding of a microorganism such as influenza (para [0063]). Therefore, the inventions of Groups I-VI lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Box V, No 2

Claims 6 and 10 lack an inventive step under PCT Article 33(3) as being obvious over Sutton in view of US 2005/0281772 A1 to Bromley et al. (hereinafter "Bromley").

Regarding claim 6, Sutton teaches the method of claim 1, including one or more of the digestive enzymes (pg 4, para 2-3) but does not specifically teach that the composition comprises avian enzymes or pig enzymes. Bromley teaches pig (swine) pancreatic digestive enzymes (para [0291]) for use in treatment of influenza (para [0435]). It would have been obvious to one of ordinary skill in the art to combine the teachings of Sutton and Bromley to utilize pig digestive enzymes for the treatment of influenza, because the use made of such enzymes as taught by Bromley would have been expected to be effective for the same infection (influenza) as taught for digestive enzymes derived from other sources as taught by Sutton.

Regarding claim 10, further to the method of claim 8, as described above, Bromley teaches that the animal source is a pig pancreas (para [0291]).

Claims 13, 14 and 38 lack an inventive step under PCT Article 33(3) as being obvious over Sutton in view of US 2009/0232789 A1 (Fallon).

Regarding claim 13, Sutton teaches the method of claim 1, including that the composition comprises proteases (pg 4, para 3, trypsin and chymotrypsin) and papain (pg 4, para 2) but does not specifically teach that the pharmaceutical composition (pg 2, para 3) comprises: amylases from about 10,000 to about 60,000 U.S.P, proteases from about 10,000 to about 70,000 U.S.P, lipases from about 4,000 to about 30,000 U.S.P., chymotrypsin from about 2 to about 5 mg, trypsin from about 60 to about 100 mg, papain from about 3,000 to about 10,000 USP units, and papaya from about 30 to about 60 mg. Fallon teaches pharmaceutical compositions (para [0022]) comprising amylases from about 10,000 to about 60,000 U.S.P (para [0036]), proteases from about 10,000 to about 70,000 U.S.P (para [0037]), lipases from about 4,000 to about 30,000 U.S.P. (para [0038]), chymotrypsin from about 2 to about 5 mg (para [0040]), trypsin from about 60 to about 100 mg (para [0041]), papain from about 3,000 to about 10,000 USP units (para [0042]), and papaya from about 30 to about 60 mg (para [0043]). It would have been obvious to one of ordinary skill in the art to combine the teachings of Sutton and Fallon to prepare a pharmaceutical composition comprising the above-described dosage ranges of amylases, proteases (chymotrypsin, trypsin, papain), lipases and papaya, because the exact formulation of components as taught by Fallon for treatment of conditions such as toxemias would have been expected to be effective for treatment of influenza as taught by Sutton, because of Sutton's teaching of effectiveness of digestive enzymes for influenza.

Regarding claim 14, Sutton teaches the method of claim 1, including compositions comprising proteases (pg 4, para 3, trypsin and chymotrypsin) and papain (pg 4, para 2) but does not specifically teach that the pharmaceutical composition (pg 2, para 3) comprises at least one protease and at least one lipase, and wherein the ratio of total proteases to total lipases (in USP units) ranges from about 1:1 to about 20:1. Fallon teaches pharmaceutical compositions (para [0022]) comprising proteases in a range of amounts from about 10,000 to about 70,000 U.S.P (para [0037]) and lipases at ranges from about 4,000 to about 30,000 U.S.P. (para [0038]). It would have been obvious to one of ordinary skill in the art to combine the teachings of Sutton and Fallon to prepare a pharmaceutical composition comprising protease:lipase ratio of 1:1 to 20:1 by utilizing amounts of proteases and lipases within the amounts taught by Fallon.

SEE CONTINUATION SHEET.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/53484

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:
Box V, Supplemental Page 1

Regarding claim 38, Sutton teaches a method of preventing infection of an individual with influenza (pg 3, para 2) or of treating an individual diagnosed with influenza (pg 3, para 2) including administering a composition (pg 4, para 4-5) comprising one or more digestive enzymes (pg 4, para 2-3) to the individual (pg 4, para 4-5) but does not specifically teach that the method comprises:
measuring a level of fecal chymotrypsin in a stool sample of the individual; comparing the level of fecal chymotrypsin with a normal fecal chymotrypsin level; and
administering a composition comprising one or more digestive enzymes to the individual if the level of fecal chymotrypsin in the individual is less than a normal fecal chymotrypsin level. Fallon teaches measuring a level of fecal chymotrypsin in a stool sample of the individual (para [0050]) and administering a composition comprising one or more digestive enzymes (para [0036]-[0042]) to the individual if the level of fecal chymotrypsin in the individual is less than a normal fecal chymotrypsin level (para [0049], Fig 4). Although Fallon does not specifically teach that the administration of digestive enzymes based on fecal chymotrypsin levels is for the treatment the treatment of influenza, it would have been obvious to one of ordinary skill in the art to combine the teachings of Sutton and Fallon to provide the digestive enzymes based on measurement of fecal chymotrypsin, because the use of chymotrypsin levels to indicate deficiencies as taught by Fallon would have been expected to motivate the skilled practitioner to utilize digestive enzymes when said levels are deficient in the patient.

Claim 11 lacks an inventive step under PCT Article 33(3) as being obvious over Sutton in view of US 5,106,616 A to McAnalley et al. (hereinafter "McAnalley"), further in view of US 2003/0104045 A1 to Virtanen et al. (hereinafter "Virtanen").

Regarding claim 11, Sutton teaches the method of claim 1 including compositions comprising proteases (pg 4, para 3, trypsin and chymotrypsin) and papain (pg 4, para 2) but does not specifically teach that the pharmaceutical composition (pg 2, para 3) comprises at least one amylase, a mixture of proteases comprising chymotrypsin and trypsin, and at least one lipase. McAnalley teaches prevention and treatment of influenza (col 12, ln 5-7) using acemannan which is more effective when its administration is enhanced by amylases (col 17, ln 6-17). Virtanen teaches that lipases (para [0070]) are useful in disruption of the influenza virus (para [0070]). It would have been obvious to one of ordinary skill in the art to combine the teachings of Sutton, McAnalley and Virtanen to provide a pharmaceutical composition comprising amylase, a mixture of proteases comprising chymotrypsin and trypsin, and at least one lipase, because each component as taught by the combination of Sutton, McAnalley and Virtanen would have been expected to be effective in disruption of influenza virus and subsequent treatment of influenza.

Claim 15 lacks an inventive step under PCT Article 33(3) as being obvious over Sutton in view of McAnalley, further in view of Virtanen, and further in view of Fallon.

Regarding claim 15, further to the method of claim 11, as described above, Sutton teaches compositions (pg 2, para 3) comprising proteases (pg 4, para 3, trypsin and chymotrypsin) and papain (pg 4, para 2) but does not specifically teach that the pharmaceutical composition (pg 2, para 3), but neither Sutton, McAnalley nor Virtanen specifically teaches that the composition comprises at least one protease and at least one lipase, and wherein the ratio of total proteases to total lipases (in USP units) ranges from about 1:1 to about 20:1. wherein the ratio of proteases to lipases ranges from about 4:1 to about 10:1. Fallon teaches pharmaceutical compositions (para [0022]) comprising proteases in a range of amounts from about 10,000 to about 70,000 U.S.P (para [0037]) and lipases at ranges from about 4,000 to about 30,000 U.S.P. (para [0038]). It would have been obvious to one of ordinary skill in the art to combine the teachings of Sutton, McAnalley, Virtanen and Fallon to prepare a pharmaceutical composition comprising protease:lipase ratio of 4:1 to 10:1 by utilizing amounts of proteases and lipases within the amounts taught by Fallon.

Claims 1-16 and 34-38 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.